9/21/2009 JB

DECLARATION UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Anuj Chauhan, Ph.D., do hereby make the following declaration:

1) My name is Anuj Chauhan, Ph.D. and I am currently an Associate Professor in the department of chemical engineering at the University of Florida. Before joining the University of Florida, I conducted post doctoral research at the University of California at Berkeley. I obtained my undergraduate degree in chemical engineering in 1993 from Indian institute of Technology in Delhi, India, which is arguably the most prestigious school in India. I obtained my doctoral degree in chemical engineering from the City University of New York in 1998. Most of my research focuses on fluid mechanics and interfacial phenomena in biomedical systems. I have published more than 40 papers and presented more than sixty papers at various national and international conferences. My research has been cited both in peer reviewed journals and in popular press including Readers Digest, Discover, CNN Headline News, etc. My research on ophthalmic drug delivery by contact lenses was cited as a Medical Breakthrough of the year by Readers Digest. I review papers for the most prestigious journals in my field such as the Journal of Fluid Mechanics, Physics of Fluids, Langmuir, Journal of Colloids and Interface Science, etc., and organize sessions and symposiums at some of the most prestigious national conferences in chemical engineering such as the AIChE and the ACS conferences. My research focuses on the areas of fundamental as well as societal impact, such as drug delivery, drug detoxification, DNA separation, etc. My research is being supported by various companies as well as the federal agencies such as NSF, NIH and NASA.

2) The Examiner has rejected claims 1, 2, 4, 5, 9, 12 and 13 under 35 U.S.C.102(e) as being anticipated by Resnick [US 2002/0141760], (hereinafter Resnick).

3) Resnick was filed on March 29, 2001; published on October 3, 2002; and abandoned on May 17, 2004 for failure to respond to office action.

4) A disclosure cannot anticipate a claimed invention if it is not enabling. I believe Resnick to be a non-enabling disclosure as to the claims of the present invention.

   a) Resnick does not enable a person having ordinary skill in the art to provide extended or time release delivery of ophthalmic drugs by nanencapsulating such drugs and dispersing within a contact lens.

   b) Resnick does not teach on selecting encapsulation material dependent upon ophthalmic drug characteristics.

   c) Resnick does not teach the selection of a hydrophobic encapsulation material generally or a microemulsion specifically for a hydrophobic ophthalmic drug.

   d) Resnick does not teach the selection of a hydrophilic encapsulation material generally or a liposome specifically for a hydrophilic ophthalmic drug

e) Resnick does not teach on the issue of duration of release. Specifically, while Resnick refers generally to time-released substances there is no disclosure directed to controlling this release rate.

f) Resnick does not teach that the particles have to be designed specifically for a given drug such that they attenuate the drug release rates from the lens.

g) Resnick does not teach substantially uniformly dispersing the nanoencapsulated ophthalmic drug throughout the contact lens.

h) Resnick does not teach that sufficiently low nanoparticle size and loading results in a transparent lens.

i) Resnick does not teach a preferred drug-laden nanoparticle size.

j) Resnick does not teach that in the case of particle laden lenses, particles control the long time release rates, and that the time of release is relatively independent of the lens thickness.

k) Resnick teaches neither release rate time scales nor mathematical formulas defining same.

l) Resnick does not teach means of controlling the drug delivery rates such as tailoring the microstructure of the hydrogel and manipulating the size, concentration and structure of the nanoparticles and the concentration of the drug in the particles.

m) Resnick does not disclose an amount of nanoparticles from about 1 to about 5%, by weight, based on the weight of the contact lens, as defined by claim 3.

n) Resnick does not provide instruction as to the main issues relevant to transparency including particle size, loading and refractive index contrast.

o) The Examples provided by Resnick in Figures 1-3 illustrate systems that would not be transparent because of the high degree of loading evident in the figures; thus teaching away from the present invention.

5) The following summarizes the state of the art knowledge related to ophthalmic drug delivery by contact lenses:

a) Both mathematical models and clinical data suggest that the bioavailability for ophthalmic drug delivery using contact lenses can be as large as 50%[a]. There have been a number of attempts in the past to use contact lenses for ophthalmic drug delivery; however most of these focused on soaking hydrophilic lenses in a drug solution followed by insertion into the eye[b-g]. The major problem of loading drug by this method is that in most cases the loading capacity of the soaked contact lenses is inadequate. An additional problem that can occur when absorbing drugs in hydrophilic contact lens is that the preservatives included in the drug are often preferentially absorbed in the lens and the preservative can be selectively absorbed to a level that is toxic while that of the drug may be below effective levels[g].

b) A number of researchers have polymerized the monomers that comprise the hydrogel, in presence of the encapsulated proteins, cells and drugs to entrap these species in a hydrogel matrix[h-m]. Although such direct loading of drug into the lenses can allow higher loadings of the drugs, it can result in an activity loss during polymerization. Furthermore, a majority of the drug can diffuse from the lenses into the packaging

medium and the drug retained in the lens can diffuse from the lens rapidly after insertion into the eye.

c) To address these issues Gulsen and Chauhan proposed the development of nanoparticle laden gels that can load substantial amount of drug to the gel which can be released at a controlled rate from the nanoparticles[n-s]. To this date, our papers represent the only peer reviewed publications in this area. In these papers we have demonstrated the following main issues that are not obvious to a person of ordinary skill:

   i) Choosing the correct type and size of the nanoparticles is critical in designing contact lenses that are transparent and yet release drugs for an extended period of time[n-s]. For instance we showed the some particles get destabilized during polymerization leading to a loss of transparency[o]. Also we showed that hydrophobic particles such as microemulsions and micelles are necessary for obtaining sufficient loading and extended release from the particle-laden contact lenses[n-s].

   ii) If the particles do not have adequately large partition coefficient for the drug, a majority of the drug molecules will partition into the gel matrix outside the particles during packaging leading to a rapid burst release after the lens in put on the eye. This issue differentiates a contact lens from several other biomedical devices for extended drug delivery. We teach the importance of choosing particles with suitable physical properties in our patent, and in our papers, while this critical issue is neglected by Resnick.

d) The main purpose of adding particles in the contact lenses is to increase the duration of release. To accomplish this objective, it is important to design particles so that the time scale of release from the particles is slower than that for the lens matrix[o]. Resnick does not teach the importance of choosing particles that release the drug slowly. In fact, published literature shows that 5 μm microspheres, which are a type of particles taught by Resnick release drugs for only about 10 hours[l]. Thus nanoparticles of PMMA will likely release drugs for a significantly shorter than 10 hours and are thus not suitable for use in contact lenses. Resnick also discloses Geltran® and Kelco® as potential polymers for the microparticles but we were unable to obtain these materials to test the release profiles from microparticles of these polymers. Also we found no data in literature to prove that microparticles of these materials can provide extended release.

6) To summarize, our patent and publications teach several issues related to choice of materials for the particles that were neglected by Resnick. These issues are critical to designing an extended drug delivering contact lens, and we arrived at our conclusions after significant experimentation which is detailed in the patents and in the following exemplary publications.

a) Li CC, Chauhan A. Modeling ophthalmic drug delivery by soaked contact lenses. Ind Eng Chem Res 2006;45:3718-3734.

b) Hillman JS. Management of acute glaucoma with pilocarpine-soaked hydrophilic lens. Br J Ophthalmol 1974;58:674-679.

c) Ruben M, Watkins R. Pilocarpine dispensation for the soft hydrophilic contact lens. Br J Ophthalmol 1975;59:455-458.

d) Arthur BW, Hay GJ, Wasan SM, Willis WE. Ultrastructural effects of topical timolol on the rabbit cornea - outcome alone and in conjunction with a gas permeable contact-lens. Arch Ophthalmol 1983;101:1607-1610.

e) Wilson MC, Shields MB. A comparison of the clinical variations of the iridocorneal endothelial syndrome, Arch Ophthalmol 1989;107:1465-1468.

f) Schultz CL, Nunez IM, Silor DL, Neil ML. Contact lens containing a leachable absorbed material. US Patent No. 5723131, 1998.

g) Schultz CL, Mint JM. Drug delivery system for antiglaucomatous medication. US Patent No.6410045, 2002.

h) Elisseeff J, McIntosh W, Anseth K, Riley S, Ragan P, Langer R. Photoencapsulation of chondrocytes in poly(ethylene oxide)-based semi-interpenetrating networks. J Biomed Materi Res 2000;51:164-171.

i) Ward JH, Peppas NA. Preparation of controlled release systems by free-radical uv polymerizations in the presence of a drug. J Control Release 2001;71:183-192.

j) Scott RA, Peppas NA. Highly cross-linked, PEG-containing copolymers for sustained solute delivery. Biomaterials 1999;20:1371-1380.

k) Podual K, Doyle FJ, Peppas NA. Preparation and dynamic response of cationic copolymer hydrogels containing glucose oxidase. Polymer 2000;41:3975-3983.

l) Colombo P, Bettini R, Peppas NA. Observation of swelling process and diffusion front position during swelling in hydroxypropyl methyl cellulose (hpmc) matrices containing a soluble drug. J Control Release 1999;61: 83-91.

m) Ende MTA, Peppas NA. Transport of ionizable drugs and proteins in crosslinked poly(acrylic acid) and poly(acrylic acid-co-2-hydroxyethyl methacrylate) hydrogels .2. Diffusion and release studies. J Control Release 1997;48:47-56.

n) Gulsen D, Chauhan A. Ophthalmic drug delivery through contact lenses. Invest Ophth Vis Sci 2004;45:2342-2347.

o) Gulsen D, Chauhan A. Dispersion of microemulsion drops in HEMA hydrogel: a potential ophthalmic drug delivery vehicle. Int J Pharm 2005;292:95-117.

p) Gulsen D, Li CC, Chauhan A, Dispersion of DMPC liposomes in contact lenses for ophthalmic drug delivery, Current eye research, 30 (12), 2005, 1071-1080.

q) Kapoor, Y, Chauhan, A, "Ophthalmic delivery of Cyclosporine A from Brij-97 microemulsion and surfactant-laden p-HEMA hydrogels", International Journal of Pharmaceutics, In Press, 10.1016/j.ijpharm.2008.05.028.

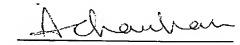
r) Kapoor, Y, Chauhan, A, "Drug and Surfactant transport in Cyclosporine A and Brij 98 laden p-HEMA hydrogels", Journal of Colloid and Interface Science, 2008, 322, 624-633.

s) Li, Chi-Chung, Abrahamson, Michael, Kapoor, Y, Chauhan, A, "Timolol transport from microemulsions trapped in HEMA gels", Journal of Colloid and Interface Science, 315, 2007, 297-306.

t) M. Sairam, V. Ramesh Babu, K. S. V. Krishna Rao, T. M. Aminabhavi, Poly(methylmethacrylate)-Poly(vinyl pyrrolidone) Microspheres as Drug Delivery Systems: Indomethacin/ Cefadroxil Loading and In Vitro Release Study, Journal of Applied Polymer Science, Vol. 104, 1860–1865 (2007).

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: August _11_, 2008

By: 

Anuj Chauhan, Ph.D.